Remarks

Upon entry of the foregoing amendment, claims 18-28 and 30-33 are pending in the application, with claim 18 being the sole independent claims. Claims 1-17 and 29 were previously cancelled. Claims 18-20 and 27 are amended. In particular, R^7 has been amended in the claims to recite hydrogen, certain alkoxyalkyl and 4-(difluoromethyl)-2-methyl-1,3-thiazol-2-yl in claims 18-20 and 27. The definition of R^7 in claim 27 has been amended to recite "methoxymethyl." Support for the amendments to claims 20 and 27 is found through out the specification as filed, *e.g.*, Table 1, page 42, compound Example 9. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Supplemental Information Disclosure Statement

Applicants note that a First Supplemental Information Disclosure Statement is submitted accompanying this Amendment and Reply. Applicants respectfully request the Examiner initial and return a copy of Information Disclosure Statement Forms.

II. Provisional Nonstatutory Obviousness-type Double Patenting Rejections

Claims 18-25, 27, 28 and 30-33 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-4 and 6-8 of co-pending Appl. No. 11/661,092 ("the '092 application"); and

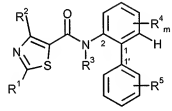
over claims 1-4 and 6-8 of co-pending 11/661,100 ("the '100 application"). Applicants respectfully traverse these rejections as they may allegedly apply to the amended claims.

According to the M.P.E.P., "the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination." *See* M.P.E.P. § 804.II.B.1. In *KSR International v. Teleflex, Inc.*, 550 U.S. 398 (2007), the United States Supreme Court noted that the key to support any rejection under 35 U.S.C. § 103(a) is the clear articulation of reason(s) why the claimed invention would have been obvious.

A. Rejection over the '092 Application

Presently pending claim 1 of the '092 application recites:

1. A compound of Formula (I)



(I),

where

. . .

R^4 is halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio or C_1-C_4-halogenalkyl having 1 to 9 halogen atoms selected from the group consisting of fluorine, chlorine and bromine,

m is 1 or 2, and when m is 2, the R^4 moieties can be the same or different,

. . . .

Each of claims 2-4 and 6-8 of the '092 application depends directly or indirectly from claim 1, and thus contains each and every limitation of claim 1. As such, each of claims 1-4 and 6-8 of the '092 application requires a *R^4-substituted* aniline group (ring

carbon atom(s) substituted by halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio or C_1-C_4-halogenalkyl), whereas claims 18-25, 27, 28 and 30-33 of the captioned application requires a *non-substituted* aniline group. Thus, contrary to the Examiner's assertion, the compounds of captioned claimed invention are structurally dissimilar to the compounds of the '092 application.

In making the rejection, the Examiner cited *In re Lincoln*, 53 USPQ 40 (CCPA 1942); *In re Druey*, 138 USPQ 39 (CCPA 1963); *In re Wood*, 199 USPQ 137 (CCPA 1978); and *In re Lohr*, 137 USPQ 548 (CCPA 1963) for the proposition that "the substitution of a lower alkyl for a hydrogen atom on a known compound is not a patentable modification absent unexpected or unobvious results." As discussed in detail *infra*, since *KSR*, the courts have addressed the requirements for a determination of obviousness in the chemical compound area. *See Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007); *Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.*, 533 F.3d 1353 (Fed. Cir. July 21, 2008); and *The Procter & Gamble Company v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989 (Fed. Cir. May, 2009). Under these modern decisions, in addition to structural similarity between the compounds, an Examiner must identify a prior art compound as a "lead compound" and provide rationale to modify that lead compound. In the captioned application, even assuming that the compounds of captioned claimed invention were structurally similar to the compounds of the '092 application, the Examiner has not provided adequate rationale why one of ordinary skill in the art would select the compounds the '092 application, and remove the substituent(s) from the aniline group of the compounds the '092 application, to arrive at the compounds of present invention. Accordingly, claims 18-25, 27, 28 and

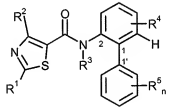
30-33 are not obvious over claims 1-4 and 6-8 of the '092 application. Applicants respectfully request that the rejection be withdrawn.

In addition, the captioned application has an effective filing date of September 26, 2003, whereas the '092 application has an effective filing date of August 13, 2005. Thus, the captioned application is an "earlier filed application." In view the above amendment and following remarks, the captioned application is in condition of allowance, expect for the provisional nonstatutory obviousness-type double patenting rejection ("the double patenting rejection"). Since the double patenting rejection would be the only rejection remaining in the captioned earlier filed application, the Examiner should withdraw the double patenting rejection in the captioned application without need of a terminal disclaimer. M.P.E.P § 804 I.B.1.

B. Rejection over the '100 Application

Presently pending claim 1 of the '100 application recites:

1. A compound of Formula (I)



(I),

where

. . .

R^4 is halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio or C_1-C_4-halogenalkyl having 1 to 9 halogen atoms selected from the group consisting of fluorine, chlorine and bromine,

. . . .

Each of claims 2-4 and 6-8 of the '100 application depends directly or indirectly from claim 1, and thus contains each and every limitation of claim 1. As such, each of claims 1-4 and 6-8 of the '100 application requires a R^4-*substituted* aniline group, whereas claims 18-25, 27, 28 and 30-33 of the captioned application requires a *non-substituted* aniline group. For the same reasons stated above, claims 18-25, 27, 28 and 30-33 are not obvious over claims 1-4 and 6-8 of the '100 application. Applicants respectfully request that the rejection be withdrawn.

In addition, the captioned application has an effective filing date of September 26, 2003, whereas the '100 application has an effective filing date of August 13, 2005. Thus, the captioned application is an "earlier filed application." For the same reasons stated above, the Examiner should withdraw the provisional nonstatutory obviousness-type double patenting rejection in the captioned application without need of a terminal disclaimer. M.P.E.P § 804 I.B.1.

III. Rejection under 35 U.S.C. § 103(a)

Claims 18-25, 27 and 30-33 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Walter *et al.* (WO02/059086) ("Walter") alone, or in combination with Kanji *et al.* (Japanese Pat. Appl. Pub. No. JP 08/176112) ("Kanji"). Applicants respectfully traverse this rejection.

A. Claims 18-25, 27 and 30-33 Are Not Prima Facie Obvious Over the Cited References

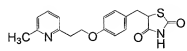
In making the rejection, the Examiner asserted that:

> Applicant claims thiazole compounds. **Walter et al.** teach thiazole compounds which are structurally similar to the instant claimed

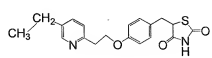
> compounds. See the entire disclosure of Walter et al., particularly pages 1, 2 and 8-16; and especially Compounds Nos. 4.19, 4.20, 4.26, 4.27 and 4.29 (page 32), Compounds Nos. 4.31, 4.32, 4.38, 4.39, 4.43 and 4.44 (page 33); Compound No. 7.03 (page 39); and Compound Nos. 7.08, 7.15, 7.18 and 7.20 (page 40). . . .
>
> * * *
>
> Further, **Kanji et al.** teach the interchangeability of the various substitutes attached to the nitrogen of the carboxanilide group (see the definition of R1 in Kanji et al in paragraph [0009]) in thiazole compounds that are useful as microbicidal agents.
>
> * * *
>
> The indiscrimination selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (1964). The motivations to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. . . .

(Office Action, pages 10-13 (emphasis original).) Applicant respectfully disagree.

Since *KSR*, the Federal Circuit has rendered several decisions in which the obviousness of a chemical compound was at issue. *Takeda* represents the Federal Circuit's first post-*KSR* decision in the chemical compound area. In *Takeda*, the court found that pioglitazone was not obvious in view of prior art that disclosed "compound b" because a person of ordinary skill in the art would not have selected compound b as a lead compound for an anti-diabetic drug, then modified it in the particular manner as alleged by the defendant. The chemical structures of pioglitazone and compound b are shown below:



compound b



pioglitazone

The Court held that:

> In addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of "adequate support in the prior art" for the change in structure.
>
> * * *
>
> Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound.

492 F.3d at 1356 and 1357 (internal citation omitted).

In *Eisai*, the court began its analysis by summarizing its chemical obviousness jurisprudence developed after *KSR*. *See Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.*, 533 F.3d 1353 (Fed. Cir. July 21, 2008).

The court stated that for a chemical compound patent,

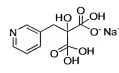
> [o]bviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound [citing Takeda]. In keeping with the flexible nature of the obviousness inquiry [citing *KSR*], the requisite motivation can come from any number of sources and need not necessarily be explicit in the art.

533 F.3d at 1357 (internal citations omitted).

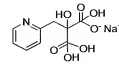
The *Takeda* and *Eisai* decisions made clear that in order to establish a *prima facie* case obviousness of a new compound, one must identify some reason that would lead a chemist to modify a lead compound.

This legal standard was reaffirmed with respect to the patentability of positional isomers in *The Procter & Gamble Company v. Teva Pharm. USA, Inc.*, 566 F.3d 989 (Fed. Cir. May, 2009) wherein the Federal Circuit held that 3-pyr etidronate (risedronate)

was not obvious in view of prior art that disclosed 2-pyr etidronate. 566 F.3d at 995. The chemical structures of 3-pyr etidronate and 2-pyr etidronate are shown below:



risedronate



2-pyr etidronate

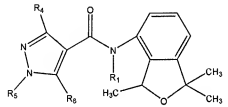
Applicants submit that, in light of the case law relating to chemical compound patents, presently pending claims 18-25, 27 and 30-33 are not *prima facie* obvious over Walter alone, or in combination with Kanji, because the Examiner has not provided a reason why a chemist would select Walter Compound Nos. 4.19, 4.20, 4.26, 4.27, 4.29, 4.31, 4.32, 4.38, 4.39, 4.43, 4.44, 7.03, 7.08, 7.15, 7.18 and 7.20 for further modification in a particular manner to arrive at the compounds of the present invention.

Specifically, Walter discloses numerous carboxamides of formulae Ia-Ii, including 46 thiazolecarboxamide compounds of formula Ic (Walter, Table 4, at pages 31-33, Compound Nos. 4.01-4.46) and 166 pyrazolecarboxamide compounds of formulae Ia, If and Ih (Walter, Table 2, at pages 22-27, Compound Nos. 2.001-2.126; Table 7, at pages 39 and 40, Compound Nos. 7.01-7.20; and Table 9, at pages 41 and 42, Compound Nos. 9.01-9.20).

With respect to Walter's thiazolecarboxamide compounds of formula Ic (*e.g.*, Compound Nos. 4.19, 4.20, 4.26, 4.27, 4.29, 4.31, 4.32, 4.38, 4.39, 4.43 and 4.44), none of them have been tested for their fungicidal activities or other biological activities. Rather, Walter discloses good fungicidal activities of other carboxamides (*e.g.*, pyrrolecarboxamides of formulae Ib and Ii (Walter, at pages 43-45). Thus, Walter does

not provide any reason that would have prompted a person of ordinary skill in the art to select thiazolecarboxamide compounds of formula Ic (*e.g.*, Compound Nos. 4.19, 4.20, 4.26, 4.27, 4.29, 4.31, 4.32, 4.38, 4.39, 4.43 and 4.44) for further modification to arrive at the compounds of present invention.

Furthermore, contrary to the Examiner's assertion, Walter's pyrazolecarboxamide compounds of formula If (*e.g.*, Compound Nos. 7.03, 7.08, 7.15, 7.18 and 7.20) are structurally ***dissimilar*** to presently claimed compounds, as these pyrazolecarboxamides require a fused ring as shown below:



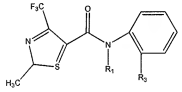
Thus, Applicants respectfully contend that Walter's Compound Nos. 7.03, 7.08, 7.15, 7.18 and 7.20 are not the closest prior art compounds. Moreover, Walter is completely silent with respect to the fungicidal activities of these compounds. As such, Walter does not provide any reason that would have prompted a person of ordinary skill in the art to select Compound Nos. 7.03, 7.08, 7.15, 7.18 and 7.20 for further modification to arrive at the compounds of present invention.

Even assuming, *arguendo*, that a person of ordinary skill in the art had a reason to select Walter's thiazolecarboxamide compounds for further modification, there are many other positions of Walter's thiazolecarboxamide compounds that could be modified and there are other substituents at R_4 and R_5 positions that could be employed (*see* Walter, at

page 2, the definitions of R_4 and R_5). The Examiner has not provided adequate rationale why one of ordinary skill in the art would modify Walter's thiazolecarboxamide compounds, in the specific manner, *i.e.*, substituting the $-CF_3$ group at R_4 position with a $-CHF_2$ group, to arrive at the compounds of present invention. The Examiner appeared to reason that one skilled in the art would have done so because some of Walter's pyrazolecarboxamide compounds of formula If (*i.e.*, Compound Nos. 7.03, 7.08, 7.15, 7.18 and 7.20) have a $-CHF_2$ group at R_4 position. However, as discussed above, these pyrazolecarboxamide compounds are structurally dissimilar to the presently claimed compounds. In addition, Walter is completely silent with respect to fungicidal or other biological activities of these pyrazolecarboxamide compounds. Nothing in Walter indicates that Compound Nos. 7.03, 7.08, 7.15, 7.18 and 7.20, which have a $-CHF_2$ group at R_4 position, are more effective fungicides as compared to the rest of Walter's pyrazolecarboxamide compounds of formula If, which a have $-CF_3$ group at R_4 position.

According to the M.P.E.P., "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." *See* M.P.E.P. § 2142. As discussed above, Walter's thiazolecarboxamide compounds have not been tested for their biological activities. Thus, the facts presented in Walter would not have led one of ordinary skill in the art to select Walter's thiazolecarboxamide compounds for further modification to arrive at presently claimed compounds. As such, Applicants contend that the Examiner merely selected Walter's thiazolecarboxamide compounds based on impermissible hindsight.

Kanji does not cure the deficiencies of Walter. Kanji discloses numerous carboxamides of formula (1) (*see* English language translation of Kanji, at pages 1 and 2). At most, Kanji discloses thiazolecarboxamide compounds of formula:



in which R_1 is COR_4, $CONHR_5$, OR_6 or R_7.

(*See* Kanji, at page 1)

The Examiner stated that Kanji "was relied on for its teaching of the substituents defined by the R_1 variable, and not the possible subtituents on the thiazole ring." (Office Action, pages 17 and 18.) As such, and as the Examiner acknowledged, Kanji does not provide adequate rationales of modifying thiazolecarboxamide compounds disclosed in Walter and Kanji, in the specific manner, *i.e.*, substituting the $-CF_3$ group with a $-CHF_2$ group on thiazole ring, to arrive at the compounds of present invention.

In sum, claims 18-25, 27 and 30-33 are not *prima facie* obvious over Walter alone, or in combination with Kanji, because Walter and Kanji do not provide any reason to select thiazolecarboxamide compounds for further modification in a specific manner to arrive at compounds of present invention. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

B. The Evidence of Superior Fungicidal Activities of Presently Claimed Compounds Rebuts Any Prima Facie Case of Obviousness

Even assuming, *arguendo*, that a *prima facie* case of obviousness had been established, which it had not, the unexpected superior fungicidal activities of presently claimed compound (Example 9) as compared to Walter compound (Compound No. 4.32), which has been demonstrated in the Declaration of Ulrike Wachendorff-Neumann ("the Declaration") submitted on February 23, 2007, is sufficient to rebut the *prima facie* case of obviousness.

However, the Examiner asserted that:

> [T]he Declaration under 37 CFR 1.132 filed February 23, 2007 is insufficient to overcome the rejection of claims 18-25, 27 and 30-33 based upon 35 USC §103 over Walter et al. {WO 02/059086}, taken alone, or in combination with Kanji et al. {JP 08/176112} as set forth in the last Office action because the showing is not commensurate in scope with the instant claims. . . .
>
> Although the definition of the instant R^6 variable has now been limited to represent $-COR^7$ or COR^8R^9 per the amendment filed October 1, 2009, the instant R^7 variable can represent a number of susbstituents, not only C_1-C_4-alkoxy-C_1-C_4-alkyl as found in instant Example 9, but also a C_1-C_8-alkyl and a C_1-C_8-alkoxy, which overlap with the teachings in Walter et al. . . . Therefore the showing of unexpected results is insufficient since the showing is not commensurate in scope with the instant claimed invention.

(Office Action, pages 3-6.) Applicants respectfully disagree.

However, solely to expedite allowance of the claims, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 18 to recite R^7 being hydrogen, C_1-C_4-alkoxy-C_1-C_4-alkyl or 4-(difluoromethyl)-2-methyl-1,3-thiazol-2-yl. R^7 no longer includes, *inter alia*, alkyl or alkoxy. Accordingly, the Declaration is sufficient to overcome the rejection under 35 U.S.C. §103(a), even assuming that a *prima facie* case of

obviousness had been established, as the showing of unexpected results therein is commensurate with the scope of claim 18 as currently presented. Applicants respectfully request that the rejection be withdrawn.

V. Allowable Subject Matter

The Examiner has indicated that claim 26 is allowable if rewritten in independent form including all of the limitations of the base claim (claim 18). For the reasons stated above, Applicants respectfully submit that the base claim 18 as currently presented is allowable, and thus, claim 26 is allowable without rewritten in independent form.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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